

CLAIMS

1. A method for generating a specific binding partner to a (poly)peptide which is encoded by a nucleic acid sequence comprised in a genomic DNA fragment or an expressed sequence tag (EST) comprising:
 - a) expressing a nucleic acid molecule encoding a fusion protein in a host cell under conditions that allow the formation of inclusion bodies comprising said fusion protein, wherein said fusion protein comprises
 - aa) a (poly)peptide/protein fusion partner which is deposited in inclusion bodies when expressed in said host cell under said conditions, and
 - ab) said (poly)peptide;
 - b) isolating said inclusion bodies; and
 - c) generating a specific binding partner that binds specifically to said (poly)peptide.
2. The method of claim 1, wherein said fusion protein comprises said fusion partner as N-terminal portion and said (poly)peptide as C-terminal portion.
3. The method of claims 1 or 2, wherein said fusion protein further comprises a (poly)peptide linker linking said fusion partner and said (poly)peptide.
4. The method of claim 3, wherein said linker comprises a cleavage signal.
5. The method of any one of claims 1 to 4, wherein said genomic DNA fragment or said EST is obtained from a prokaryotic organism or from a virus.
6. The method of claim 5, wherein said prokaryotic organism or virus is a pathogen.
7. The method of any one of claims 1 to 4, wherein said genomic DNA fragment or said EST is obtained from a eukaryotic organism.
8. The method of claim 7, wherein said genomic DNA fragment or EST is obtained from a non-mammalian species.

9. The method of claim 7, wherein said genomic DNA fragment or EST is obtained from a mammalian species.
10. The method of claim 9, wherein said mammalian species is human.
11. The method of any one of claims 1 to 10, wherein said nucleic acid is expressed under conditions allowing over-expression of said fusion protein.
12. The method of any one of claims 1 to 11, wherein said host cell is a eukaryotic cell.
13. The method of claim 12, wherein said eukaryotic cell is a yeast or insect cell.
14. The method of any one of claims 1 to 11, wherein said host cell is a prokaryotic cell.
15. The method of claim 14, wherein said prokaryotic cell is a bacterial cell.
16. The method of claim 15, wherein said bacterial cell is an *E. coli* cell.
17. The method of claims 15 or 16, wherein said fusion protein is expressed in the cytosol.
18. The method of claim 17, wherein said fusion partner contains at least one disulfide bond.
19. The method of claims 17 or 18, wherein said fusion partner is a secreted protein, and wherein said nucleic acid does not comprise a nucleic acid sequence encoding a signal sequence for the transport of the fusion protein to the periplasm.
20. The method of any one of claims 1 to 19, wherein said fusion partner is an endogenous (poly)peptide/protein of said host cell.
21. The method of any one of claims 1 to 19, wherein said fusion partner is a (poly)peptide/protein foreign to said host cell.

22. The method of any one of claims 1 to 21, wherein said fusion partner is taken from the list of *E. coli* maltose-binding protein, *E. coli* RNase II, *E. coli* alkaline phosphatase, *E. coli* phospholipase A, *E. coli* β -lactamase, *E. coli* thioredoxin, human procathepsin B, porcine interferon, and T5 DNA polymerase.
23. The method of claim 21, wherein said host cell is *E. coli* and said fusion partner comprises the first N-terminal domain of the geneIII protein of a filamentous phage.
24. The method of claim 23, wherein said fusion partner consists of amino acids 1 to 82 of the geneIII protein.
25. The method of any one of claims 1 to 24, wherein step b) further comprises the step of (i) solubilising said fusion protein under suitable conditions.
26. The method of claim 25, wherein step b) further comprises the step of (ii) refolding said fusion protein under suitable conditions.
27. The method of claims 25 or 26, wherein said fusion protein further comprises a (poly)peptide linker linking said fusion partner and said (poly)peptide, wherein said linker comprises a cleavage signal, and wherein step b) further comprises the steps of (iii) cleaving said fusion protein between said fusion partner and said (poly)peptide, and (iv) isolating said (poly)peptide in free form.
28. The method of any one of claims 25 to 27, further comprising the step of purifying said fusion protein or said (poly)peptide in free form.
29. The method of any one of claims 1 to 28, wherein said specific binding partner is an immunoglobulin or a fragment thereof.
30. The method of claim 29, wherein said immunoglobulin is generated by (i) immunisation of an animal with said inclusion bodies, said fusion protein or said (poly)peptide, and (ii) by selecting an immunoglobulin produced by said animal which specifically binds to said inclusion bodies, said fusion protein or said (poly)peptide.

31. The method of claim 29, wherein said immunoglobulin or fragment thereof is generated by selecting a member of a recombinant library of immunoglobulins or fragments thereof which specifically binds to said inclusion bodies, said fusion protein or said (poly)peptide.
32. The method of claim 31, wherein said library is displayed on the surface of a replicable genetic package.
33. The method of claim 32, wherein said replicable genetic package is a filamentous phage.
34. A nucleic acid molecule encoding a fusion protein comprising aa) the first N-terminal domain of the geneIII protein of filamentous phage and ab) a (poly)peptide which is encoded by a nucleic acid sequence comprised in a genomic DNA fragment or an expressed sequence tag (EST), wherein said nucleic acid molecule does not comprise a nucleic acid sequence encoding a signal sequence for the transport of the fusion protein to the periplasm of a bacterial host cell.
35. A vector comprising a nucleic acid molecule of claim 34.
36. The vector of claim 35 which is an expression vector.
37. A host cell comprising a nucleic acid of claim 34 or a vector of claims 35 or 36.
38. The host cell of claim 37 which is an E.coli cell.
39. The use of a fusion protein comprising the first N-terminal domain of the geneIII protein of filamentous phage as fusion partner for the expression of a (poly)peptide/protein fused to said fusion partner, wherein said fusion protein is obtained in the form of inclusion bodies.
40. A method for the expression of a (poly)peptide/protein comprising:

- a) expressing a nucleic acid molecule encoding a fusion protein in a host cell under conditions that allow the formation of inclusion bodies comprising said fusion protein, wherein said fusion protein comprises
 - aa) the first N-terminal domain of the geneIII protein of filamentous phage, and
 - ab) said (poly)peptide/protein.
41. The method of claim 40 further comprising the steps of
- b) isolating said inclusion bodies; and
 - c) solubilising said fusion protein under suitable conditions.